

CLAIMS

1. A conjugated composition comprising:
a fragment of HIV-1 Vpr comprising amino acid sequence 17-36
and/or 59-84 or a non-HIV-1 Vpr protein comprising amino acids amino acids 17-36 and
5 59-84 conjugated to a therapeutic compound.
2. The conjugated composition of claim 1 wherein said fragment of HIV-1 Vpr
or said non-HIV-1 Vpr protein further comprises a polycationic amino acid sequence.
3. The conjugated composition of claim 1 wherein said therapeutic compound
is a DNA vaccine plasmid conjugated to said fragment of HIV-1 Vpr or said non-HIV-1
10 Vpr protein by ionic bonds.
4. The conjugated composition of claim 1 wherein said fragment of HIV-1 Vpr
or said non-HIV-1 Vpr protein further comprises a polycationic amino acid sequence and
said therapeutic compound is a nucleic acid molecule which is conjugated to said
polycationic amino acid sequence by ionic bonds.
- 15 5. The conjugated composition of claim 1 wherein said compound is an antisense
molecule.
6. The conjugated composition of claim 1 wherein said compound is an antisense
oligonucleotide
7. A method of delivering a compound to the nucleus of a cell comprising the
20 step of:
contacting said cell with a conjugated compound that is either said
compound conjugated to a fragment of HIV-1 Vpr protein comprising amino acids 17-36
and/or 59-84 or said compound conjugated to a non-HIV-1 Vpr protein comprising amino
acids 17-36 and/or 59-84 of HIV-1 Vpr protein; wherein said conjugated compound is
25 taken up by said cell and localized to the nucleus of said cell.

- 44 -

8. The method of claim 7 wherein said compound is a DNA molecule.
9. The method of claim 7 wherein said compound is a plasmid DNA molecule.
10. The method of claim 7 wherein said compound is an antisense molecule.
11. The method of claim 7 wherein said compound is an antisense oligonucleotide
- 5 12. A fragment of HIV-1 Vpr comprising amino acid sequence 17-36 and/or 59-84 or a non-HIV-1 Vpr protein comprising amino acids 17-36 and/or 59-84 of HIV-1 Vpr protein.
13. A method of inhibiting cell proliferation comprising the step of:
arresting said cell's advance in the cell cycle by contacting said cell
- 10 with
a fragment of HIV-1 Vpr protein comprising amino acids 19-35
and/or 74-89; or
a non-HIV-1 Vpr protein comprising amino acids 19-35 and/or
74-89 of HIV-1 Vpr protein; or
- 15 a nucleic acid molecule that encodes a fragment of HIV-1 Vpr
protein comprising amino acids 19-35 and/or 74-89; or
a nucleic acid molecule that encodes a non-HIV-1 Vpr protein
comprising amino acids 19-35 and/or 74-89 of HIV-1 Vpr protein;
wherein said fragment of HIV-1 Vpr or non-HIV-1 Vpr protein
- 20 is taken up by said cell or
said nucleic acid molecule that encodes a fragment of HIV-1
Vpr protein or said nucleic acid molecule that encodes said non-HIV-1 Vpr protein is taken
up by said cell and expressed to produce said fragment of HIV-1 Vpr or non-HIV-1 Vpr
protein in said cell, and said fragment of HIV-1 Vpr or non-HIV-1 Vpr protein inhibits
- 25 said cell from advancing in said cell cycle.

- 45 -

14. A method of treating an individual who has a hyperproliferative comprising the step of administering to said individual in an amount effective to inhibit cell proliferation a composition comprising:

5 a fragment of HIV-1 Vpr protein comprising amino acids 19-35 and/or 74-89; or

a non-HIV-1 Vpr protein comprising amino acids 19-35 and/or 74-89 of HIV-1 Vpr protein; or

a nucleic acid molecule that encodes a fragment of HIV-1 Vpr protein comprising amino acids 19-35 and/or 74-89; or

10 a nucleic acid molecule that encodes a non-HIV-1 Vpr protein comprising amino acids 19-35 and/or 74-89 of HIV-1 Vpr protein;

wherein said fragment of HIV-1 Vpr or non-HIV-1 Vpr protein molecule is taken up by proliferating cells of said individual or

15 said nucleic acid molecule that encodes a fragment of HIV-1 Vpr protein or said nucleic acid molecule that encodes said non-HIV-1 Vpr protein is taken up by a proliferating cell of said individual and expressed to produce said fragment of HIV-1 Vpr or non-HIV-1 Vpr protein molecule in said cell, and said fragment of HIV-1 Vpr or non-HIV-1 Vpr protein molecule inhibit said cell from advancing in said cell cycle.

15. A fragment of HIV-Vpr comprising amino acid sequence or a non-HIV-1 Vpr
20 protein comprising amino acids 19-35 and/or 74-89 of HIV-1 Vpr protein.

16. A pharmaceutical composition comprising:

a fragment of HIV-Vpr or a non-HIV-1 Vpr protein according to claim
15; and

25 a pharmaceutically acceptable carrier.

17. A nucleic acid molecule that encodes a fragment of HIV-1 Vpr protein comprising amino acids 19-35 and/or 74-89; or a nucleic acid molecule that encodes a non-HIV-1 Vpr protein comprising amino acids 19-35 and/or 74-89 of HIV-1 Vpr protein.

- 46 -

18. A nucleic acid molecule according to claim 17 wherein said nucleic acid molecule is a plasmid.
19. A nucleic acid molecule according to claim 17 wherein said nucleic acid molecule is a viral genome.
- 5 20. A pharmaceutical composition comprising:
a nucleic acid molecule according to claim 17; and
a pharmaceutically acceptable carrier.
21. A method of identifying compounds that inhibit Vpr protein binding to the p6 domain of p55 or to p6 protein which comprises the steps of:
- 10 a) contacting a fragment of HIV-1 Vpr comprising amino acid sequence 17-36 or a non-HIV-1 Vpr protein comprising amino acids 17-36 of HIV-1 Vpr protein with a protein comprising an HIV-1 Gag protein p6 domain in the presence of a test compound,
b) determining the level of binding between said fragment of HIV-1 Vpr or said non-HIV-1 Vpr protein and said protein comprising an HIV-1 Gag p6 domain and
- 15 c) comparing that level of binding to the level of binding between said fragment of HIV-1 Vpr or said non-HIV-1 Vpr protein and said protein comprising an HIV-1 Gag p6 domain contacted in the absence of a test compound.
22. The method of claim 21 wherein said protein comprising an HIV-1 Gag p6 domain is p55.
- 20 23. The method of claim 21 wherein said protein comprising an HIV-1 Gag p6 domain is p6.
24. A kit for performing the method of identifying compounds which inhibit Vpr protein binding to p55's p6 domain or to p6 protein of claim 21, said kit comprising:
a) a first container comprising a fragment of HIV-1 Vpr comprising amino
- 25 acid sequence 17-36 or a non-HIV-1 Vpr protein comprising amino acids 17-36 of HIV-1 Vpr protein; and

- 47 -

b) a second container comprising a protein comprising an HIV-1 Gag protein p6 domain.

25. A fusion protein comprising comprises a Vpr amino acid sequence 17-36 and non-Vpr amino acid sequences.

5 26. The fusion protein of claim 25 wherein said non-Vpr amino acid sequences are biologically active protein sequences.

27. Drug delivery particles comprising fusion proteins of claim 25.